nary infusion of escalating doses of selected, autologous, bone marrow AC133 cells are safe for use in humans with chronic ischemia. We anticipate that these continued laboratory studies will provide sound scientific rationale for future phase II and III clinical studies in cardiovascular disease.

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ISOLATION AND CHARACTERIZATION OF UMBILICAL CORD BLOOD-DERIVED MULTIPOTENT STEM CELLS ARISING FROM AN ADHERENT $CD45^+/CD34^+$ CELL SUBSET

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A number of groups have reported the presence of cells with varying degrees of multi-lineage potential arising from a $CD45^-/CD34^-$ cell population with a fibroblastic morphology and characteristics consistent with mesenchymal stem cells (MSC). This study reports the identification of stem cells distinct from MSCs deriving from a plastic adherent $CD45^+/CD34^+$ population with the ability to establish stable, readily expandable clones with extensive multi-lineage potential. Differentiation protocols have been developed to induce conversion of multilineage precursor cells (MLPCs) to adipocytes, osteocytes, chondrocytes, myocytes, neural and glial cells, endothelial cells, lung epithelial cells and hepato-pancreatic precursor cells. The ability of individual clonal cell lines to differentiate into each of the described cell types demonstrates the potential to derive tissue types consistent with all three germinal layers. Molecular karyotyping and microarray analysis have shown the MLPC to be a normal diploid cell that is stable through many doublings and is a very primitive cell, not committed to specific lineages. MLPC do not spontaneously differentiate and retain their morphology and phenotype throughout culture unless specifically induced to differentiate. Early studies with extra-cellular matrices suggest a potential utility of MLPC in tissue engineering as well as a tool for target validation and toxicity testing in pharmaceutical development.

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IMMUNE RECONSTITUTION AFTER UMBILICAL CORD BLOOD TRANSPLANTATION

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Unrelated cord blood transplantation (UCBT) has been increasingly utilized for a wide variety of malignant and non-malignant conditions. HLA-mismatching between cord blood grafts and their recipients is better tolerated with a reduced risk for lethal graft versus-host disease (GVHD) despite the adoptive transfer of several million cord blood T cells/kg recipient weight. The almost exclusively naïve, antigen inexperienced cord blood T lymphocytes demonstrate functional immaturity providing the currently accepted mechanism responsible for this phenomenon. However, infections within the first 3-6 months after UCBT, remain the major cause of morbidity and mortality. We will review key aspects of neonatal immunity that reflect the immunoregulatory effects of the feto-maternal interface. Multiple control mechanism exist here impacting on both neonatal and maternal T lymphocytes that are essential to sustain immune tolerance between fetus and mother.

Our current research efforts focus on elucidating the unique biology of immune reconstitution after UCBT. Our guiding hypothesis is that the kinetics and quality of immune recovery within the first 2 months after transplant are directly related to interactions between the adoptively transferred T cells, host factors, and the presence or absence of latent viral infections. These interactions in a lymphopenic environment could influence and bias the emerging T lymphocytes and dendritic cells post-UCBT. We have extensively studied >150 children, all unrelated cord blood recipients, in our laboratory over the past years. Despite the presence of immunosuppressive agents such as Cyclosporine A and corticosteroids there is peripheral expansion and significant maturation in the T cell compartment already within the first 3 weeks after UCBT. Those experiencing or at risk for OI develop significantly faster towards an effector Th1/Tc1 phenotype and function, essential for effective control of viral, fungal infections. In addition select features of T cell activation and cytokine secretion profile can identify those who develop acute GVHD.